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Estrogen, cognition and female ageing.

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Starting from fetal life, estrogens are crucial in determining central gender dimorphism, and an estrogen-induced synaptic plasticity is well evident during puberty and seasonal changes as well as during the ovarian cycle. Estrogens act on the central nervous system (CNS) both through genomic mechanisms, modulating synthesis, release and metabolism of neurotransmitters, neuropeptides and neurosteroids, and through non-genomic mechanisms, influencing electrical excitability, synaptic function and morphological features. Therefore, estrogen's neuroactive effects are multifaceted and encompass a system that ranges from the chemical to the biochemical to the genomic mechanisms, protecting against a wide range of neurotoxic insults. Clinical evidences show that, during the climacteric period, estrogen withdrawal in the limbic system gives rise to modifications in mood, behaviour and cognition and that estrogen administration is able to improve mood and cognitive efficiency in post-menopause. Many biological mechanisms support the hypothesis that estrogens might protect against Alzheimer's disease (AD) by influencing neurotransmission, increasing cerebral blood flow, modulating growth proteins associated with axonal elongation and blunting the neurotoxic effects of beta-amyloid. On the contrary, clinical studies of estrogen replacement therapy (ERT) and cognitive function have reported controversial results, indicating a lack of efficacy of estrogens on cognition in post-menopausal women aged >or=65 years. These findings suggest the presence of a critical period for HRT-related neuroprotection and underlie the potential importance of early initiation of therapy for cognitive benefit. In this review, we shall first describe the multiple effects of steroids in the nervous system, which may be significant in the ageing process. A critical update of HRT use in women and a discussion of possible prospectives for steroid use are subsequently proposed.